cancerous growth. In the latter, as the result of the abnormal conditions in the cells which are reached by the stimuli, structural abnormalities are produced.

We have attempted to correlate the most important facts which have a bearing on the etiology of cancer. We see that while of a composite character the various factors, as far as they are known to us, have one characteristic in common: they tend to increase the proliferative energy and motility of cells which are not yet cancerous. The picture thus presented is more complex than the one which we meet in the "theories of cancer" to which so much attention has been given in the literature. In the case of a "theory of cancer" usually one or the other of the factors underlying cancer has been considered with the exclusion of all the factors. Deductions based on the histological characteristics which were usually not accessible to experimental analysis formed often the basis of such theories. Thus a simplification was attained which was more apparent than real.

Equally prominent in the literature has been the discussion whether or not a certain new formation is to be classed as a cancer. The answer given usually depended on the "theory of cancer" to which the author subscribed. A definition of a condition cannot be more definite than our knowledge of this condition; otherwise the definition produces an artificial restriction to the search for new relations. A definition is therefore perhaps of less importance than is often attached to it. It is essentially a summary of our knowledge of a phenomenon. Cancer is abnormality of growth. Primarily it is a disturbance in the equilibrium of the individual, not through toxins but through an increased proliferative activity of the cells which is usually associated with an increased motility. This increase is long continued and often permanent. It is in all probability in the large majority of cases due to changes in cell metabolism, which are of such a character that they propagate themselves. In some cases the same effect may perhaps be produced through extraneous causes, such as microörganisms.

THE TREATMENT OF THYROID AND OTHER ENDOCRIN DISTURBANCES AS VIEWED BY THE INTERNIST.[1]

By John A. Lichty, M.D.,
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Mrs. G. C., a farmer's wife, aged fifty-nine years, was brought to the hospital by her family physician. She complained of a throbbing, beating sensation in the abdomen and also of general weakness. These symptoms came on gradually in the past six months. They had their inception apparently from a nervous shock. The patient's only son had died rather suddenly following an operation for a ruptured appendix and a few days later her only grandchild died of influenza. On further inquiry it was found that nine years previously, while the patient was passing through the menopause, her only daughter died very suddenly, and that following this death she had what was then called a "nervous breakdown," a condition thought to be similar to her present attack.

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[1] Read before the Section on General Medicine of the College of Physicians of Philadelphia, December 15, 1919.

The patient was found to be 37 pounds below her usual weight. The skin was moist. The pulse-rate was 132 and easily accelerated; the heart action was violent. There was tremor of the tongue and hands. The hair was brittle and the eyes prominent. A slight bogginess of the isthmus of the thyroid could be felt. Practically every symptom of hyperthyroidism was present.

This is a familiar picture which resulted from the tragic episodes which came to the household over which the patient presided. In a rather intensive study of the case, definite evidence of an unbalanced endocrin system in which the thyroid gland was the chief factor was found. In addition to the very evident symptoms the examination brought out the fact that carbohydrate metabolism was disturbed. A subcutaneous injection of $\frac{1}{2}$ c.c. of 1 to 1000 adrenalin solution ("Goetsch test") produced a glycosuria, though it aggravated the thyroid symptoms only slightly. A carbohydrate tolerance test also brought sugar to the urine, even though there was no previous hyperglycemia demonstrable. While the patient was resting in her changed surroundings the thyroid lost its boggy feel, body weight was increased and the most prominent symptoms, especially the tachycardia and anxiety, disappeared.

This patient, aside from illustrating a large and increasing group of cases, also demonstrates how profound and disabling such symptoms may be without there being present very definite physical signs suggestive of definite pathology; and it also brings out the question whether there might not be an early stage in the course of the disturbances of the endocrin system, where a comprehension of what is taking place, or is about to take place, may lead to earlier recognition and consequently more satisfactory treatment. It is for the purpose of presenting this idea that the present consideration from the viewpoint of the internist is attempted.

It is, of course, axiomatic that if a disease is to be recognized and dealt with at its earliest inception there must exist a thorough knowledge of the etiology as well as of the pathology and of the clinical manifestations. Unfortunately of diseases and disturbances of the endocrin system we know comparatively little, practically nothing definite, of the etiology, and we have only confused ideas of the associated pathological processes. Compared with our present-day knowledge of such a well-known disease as typhoid fever we know very little about the diseases of the glands of internal secretion, and are therefore at a great disadvantage and no doubt show a great confusion of opinions. There is not yet that coördination in effort and ideas of the laboratory workers, of the clinician and of the surgeons, all of whom are intensely interested in the problems which the subject presents. In the last decade or so much information has accumulated: (1) Because of the fact that endocrin disturbances are more generally recognized by the clinician; (2) their relation to disease in general and to definite pathology is being established, and theorizing has been displaced by more earnest laboratory investigation. The recent great war with all its strain and anxiety, resulting in so-called shell-shock, effort syndrome, neurocirculatory asthenia, all of which may be manifestations of endocrin disturbance, has made the problem really acute, and it is well to pause at this time for a moment to review the present status and to consider the foundations for our faith in the procedures we are advocating when we speak of the treatment for a certain symptom-complex referred to the endocrin system. In this consideration the diseases and disturbances of the thyroid gland are of particular importance.

In such a review we must acknowledge our debt to the laboratory worker and his discoveries. It will be interesting, and probably helpful, to refer briefly to some of their epoch-making revelations, because from them will be seen at once the relation which the several glands of the endocrin system bear to each other, and it will also show where the clinician receives his greatest help and in what direction his efforts will likely prove most fruitful. Only brief reference can be made to early laboratory results which have more recently shown the coördination of the endocrin system and how delicately this system is balanced.

THE SUPRARENALS AND THEIR SPECIFIC SECRETION. It was in 1841 that Magenda told his students that he had nothing to say about the suprarenal bodies, because the capsule is no longer considered as a secreting body. Just fourteen years later (1855) Thomas Addison described the disease which bears his name, and this marked the beginning of clinical work in relation to the suprarenal glands. In 1902 J. Takamine published the work of Aldrich and himself,[2] giving a description of a crystalline compound and its clinical formula, which they isolated from the suprarenal gland. Later, Stolz, followed immediately by Abel, produced this crystalline form—adrenalin—synthetically. This substance figures largely in developing our knowledge of the interrelation of the ductless glands. With it we can produce most profound circulatory disturbances: can, under certain conditions, activate the thyroid gland and can unbalance carbohydrate metabolism. It has become a definite therapeutic agent and, administered under certain conditions, also gives diagnostic information.

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[2] Jour. Am. Med. Assn., January 18, 1902, p. 153.

THE THYMUS GLAND AND ITS RELATION TO THYROID DISTURBANCE. In his Harvey lecture in March, 1914, Halstead called attention to the belief that the thymus gland plays an important part in Graves's disease. He said: "It has been estimated, as a result of non-operative clinical examination, that in about 40 per cent. of all cases of exophthalmic goiter the thymus is present." He refers to 500 patients with Graves's disease operated with approximate cures in 60 per cent. The exophthalmos and the typical blood picture seemed the most difficult conditions to overcome, even when the major symptoms had largely subsided, but both conditions yielded when the thymus was considered properly. Halstead then refers to the relation of the thymus to the thyroid as noticed by other observers, and says, from the facts gleaned at the autopsy table, from experiments on animals and above all from the results following primary thymectomies, we have convincing evidence that the thymus gland may play an important part in Graves's disease. Two months later he referred to the treatment of the thymus gland with roentgen rays in certain selected cases of Graves's disease and reported his experience in a subsequent paper. While the coördination of the thymus and the thyroid glands, which Halstead suggested, has not proved so generally convincing as it promised, his work led to the demonstration of the effect of the roentgen rays in thyroid disease, whether through the thymus or direct on the thyroid.

An interesting case which occurred in my experience, apparently bearing upon the relation of the thymus to the thyroid, is as follows: A man whom I had known for a number of years consulted me about five years ago on account of a tickling in his throat. A physical examination showed nothing, but rather definitely prominent eyes. An examination by a nose and throat specialist was negative. The hacking cough continued, however, and was finally so severe that the patient could not lie down without bringing on a violent paroxysm of coughing. He was unable to sleep in a prone position. About this time he had a severe attack of acute tonsillitis, which was followed by tachycardia, which could not be explained except as probably due to the preceding acute infection. Graves's disease was considered, as many symptoms were suggestive. The thyroid, however, was not enlarged. A roentgen-ray examination of the chest, especially of the mediastinum, showed an enormous enlargement of the thymus gland. It is possible that this was present in a lesser degree from the first and accounted for the hacking cough. It was suggested that the acute infection led to a rapid enlargement of the thymus and that the symptoms of Graves's disease, which we then recognized clearly, were due to the effect of the thymus upon the thyroid. The symptoms, including the tickling cough, were relieved entirely by treating the thymus with roentgen-ray applications. The patient has been well now for nearly three years. A roentgen-ray examination of the mediastinum following the treatment showed a great reduction in the thymus gland. The excellent result in this case is another reason for reporting it. It is possible that the roentgen-ray applications to the thymus had a direct action upon the thyroid as well, and that the change in size of the thymus was simply coincident. I am all the more willing to consider the case in this way since reading the recent article by Drs. Edward Park and Roy D. McClure[3] in which they conclude, from an extensive review of the literature and after painstaking animal experimentation, that destruction of the thymus function fails to show an effect on the thyroid gland. While the thymus may not bear the relation to the thyroid which Halstead suggested, after all his work called attention to the effect of the roentgen rays upon the thyroid secretion, and added greatly to the therapeutics of thyroid disease.

THE PITUITARY BODY AND ITS SECRETION. The work of Marie, of Schafer and later of Howell called attention to the hypophysis cerebri, in the chain of the glands of internal secretion, as a "vitally important organ." It was not, however, until the masterly work of Cushing[4] appeared that it was at all appreciated what pathology may occur in the pituitary gland, and what clinical and what physiological disturbances may follow. There resulted from the studies of this gland, as from that of the suprarenal, another addition to our therapeutic armamentarium. The effect of pituitrin upon the gravid uterus and upon the relaxed unstriated muscles in general is well known. More recently the effect of pituitrin on urinary secretion has been brought to our attention. A striking demonstration of the effect of pituitrin on diabetes insipidus is presented in the following case: A sixteen-year-old girl consulted me on account of sleeplessness and of being occasionally mentally confused. In the course of the history it was found that the patient had a polyuria, passing as much as 5 liters of urine in twenty-four hours. She also had polydipsia. This was largely responsible for the sleeplessness. After careful investigation a diagnosis of diabetes insipidus was made. Pituitrin was given daily and in forty-eight hours the urinary output was reduced to 1½ liters. The intense thirst disappeared and sleep was natural. The symptoms were later controlled by smaller doses given less frequently. The limitations of this treatment are, of course, generally recognized, and yet it is a good example of the profound specific effect of a substance elaborated in the hypophysis cerebri. In an article in the *Quarterly Journal of Medicine* (April, 1919), Kenneway and Mottram, of the Middlesex

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[3] The Results of Thymus Extirpation, Am. Jour. Dis. Children, November, 1919.

[4] Bull. Johns Hopkins Hosp., May, 1910.

Hospital, London, recorded the antidiuretic effect of pituitrin subcutaneously injected in normal individuals as well as in those having diabetes insipidus. It would seem, however, that this observation will need further investigation.

THE PANCREAS AND ITS INTERNAL SECRETION. The role of the islands of Langerhans in relation to carbohydrate metabolism, and especially the histological changes which take place in diabetes mellitus, was first definitely brought to our attention by Opie in 1900.[5] Since that time the work upon the pancreas has been prodigious and has resulted in a more rational view of the relation of diabetes mellitus to the pancreas. McCallum[6] called attention to the actual hypertrophy of the isles in severe cases of diabetes mellitus. And later Allen[7] demonstrated definitely the relation between the disease of the pancreas, especially of the isles of Langerhans, and diabetes mellitus, and suggested a rational treatment, which Joslin, from a clinical standpoint, subsequently made practical. Allen and Joslin's work is intensely practical and is of real value to the clinician. The emphasis which Allen has put upon early recognition of physiological disturbance of the isles of Langerhans and prompt definite interference is applicable not only in diseases of other organs of the endocrin system, but may be of value in those diseases in general whose early symptoms might be easily overlooked.

It would be interesting to speak of the ovaries and their specific secretion, of the parathyroids and of other glands of the endocrin system, but I shall now direct my remarks more specifically to that laboratory work which has led the internist to more rational procedures in diseases and disturbances of the thyroid gland. The first description of thyroid disturbance by Graves, in 1835, is, of course, a matter of history, and the laboratory work which led to the extraction of a substance from sheeps' thyroid, which when given in sufficient dose reproduced the symptoms of Graves's disease. The important place which thyroid extract took as a therapeutic measure is well known to all. Very little of value has been added to the definite clinical description which characterizes Graves's first paper. I shall refer only to the recent laboratory investigations and their bearing upon our present concept of thyroid disturbances, especially in so far as early diagnosis and the treatment therefor is concerned.

THE DISTURBANCE OF BASAL METABOLISM IN HYPERTHYROIDISM. We are indebted to Du Bois[8] for first successfully calling attention to the striking change which takes place in metabolism in the thyroid case. In his paper Du Bois says that in a study of the basal metabolism in hyperthyroidism it becomes apparent there is an increase in metabolism in proportion to the severity of the disease. Very severe cases show a metabolism 75 per cent. or more above the average, severe cases 50 per cent. or more, moderately severe and mild cases show an increase of less than 50 per cent., while a few mild and several atypical cases, or cases in which operation has been performed, are within normal limits. The degree of tachycardia, goitre, exophthalmos and mental irritability are roughly proportional to the increased heat production. At least a part of the tachycardia is due to the increased metabolism, and perhaps it might be possible to reproduce the extreme tachycardia, the cardiac enlargement, emaciation and mental irritability if we are able to stimulate the metabolism of normal men for twenty hours a day over a period of months or of years.

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[5] Jour. Exper. Med., 1901.

[6] AM. JOUR. MED. SC., 1917, cxxxiii, 432.

[7] Glycosuria and Diabetes, Harvard University Press, 1913.

[8] Arch. Int. Med., 1916, xvii, 915.

These observations of Du Bois and his conclusions have become so generally recognized that it is now necessary to make metabolism observations before a diagnosis of hyperthyroidism is accepted, or at least before a reliable and safe prognosis can be made. It would be interesting to note, by a series of investigations, whether the basal metabolism is changed in any way in those early cases in which the subcutaneous injection of adrenalin seems to develop a so-called potential hyperthyroidism. Studies in metabolism are now being made in the cases of so-called effort syndrome which may result in differentiating these cases definitely from hyperthyroid cases or which may show that they manifest early symptoms of the exophthalmic goitre syndrome. I am of the opinion that the latter may be found the true interpretation, though I believe this is contrary to the opinions of those who have had large opportunity for observation in the neuropsychiatric division of the army.

Barring the slight temporary bogginess of the thyroid, the case to which we referred at the beginning of this paper, came very near corresponding to the neurocirculatory-asthenia syndrome instead of to that of hyperthyroidism. It will require more definite laboratory and clinical work before this point of differentiation can be clarified.

THE INNERVATION OF THE THYROID GLAND. This was presented in an article by Cannon,[9] entitled "Conditions Affecting the Secretions of the Thyroid Gland," in which he concluded, after describing his methods of observation, that "The nerves distributed to the thyroid cells belong to the sympathetic and not to the vagal supply and that their effects are not indirect through alterations of blood flow: indeed, that they are true secretory nerves. The thyroid gland is subject to that division of the nervous system which is brought into action in emotional excitement and which causes adrenal secretion. It is probable, therefore, that the thyroid, like the adrenal, has, normally, functions which are performed in times of critical emergency. It may be that such an emergency function is an exaggerated form of the routine activity of the gland." Cannon's work has been severely criticized, but it has stimulated research on the innervation of the thyroid and will no doubt result in bringing out the real facts, which is, of course, the object of all scientific investigation. The latest word on this subject is probably that of C. A. Mills,[10] in which he affirms the lack of secretive function of the sympathetic fibers of the thyroid gland.

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[9] Boston Med. and Surg. Jour., 1916 clv, 562.

THE ISOLATION IN CRYSTALLINE FORM OF AN IODIN COMPOUND FROM THE THYROID GLAND. In an article by Dr. E. C. Kendell, of the Mayo Clinic,[11] he announces the discovery and separation among other substances, of a purely crystalline compound containing 60 per cent. iodin. It appears to be an iodo-di-hydroxy-indol. Administration of this substance in a human being produces a rapid increase in pulse-rate, gain in vigor and increase in metabolism and nervous irritability. Given in excess, toxic symptoms are produced. The amount of iodin compound required to produce toxic effect is exceedingly small. He believes it plays an important role in the production of the symptoms of exophthalmic goitre. Kendell says, further, that in exophthalmic goitre two abnormal conditions exist: (*a*) The secretory capacity of the gland is greatly increased, and (*b*) the reservoir capacity of the gland is greatly decreased.

The use of iodin in goitre is a procedure to which our attention was called many years ago. The results of Kendell's work impress one very much with Marine and Kimball's observations, as reported in the *Archives of Internal Medicine*, July, 1918, "The Prevention of Simple Goitre in Man." They had the opportunity of observing 1080 girls in the Akron public schools, with reference to the effect of administering iodin. They concluded (1) that simple goitres may be prevented by the administration of small amounts of iodin; (2) simple goitres disappear or are markedly decreased by the use of a small amount of iodin given internally; (3) there is no danger of producing toxic conditions, such as Basedow's disease; (4) simple goitre is probably the easiest of all known diseases to prevent.

A TEST FOR DETERMINING "POTENTIAL HYPERTHYROIDISM." Dr. Emil Goetsch has suggested a unique procedure for determining the potential possibilities of the thyroid in the particular individual. The principle and procedure of this test are no doubt familiar to all. One-half cubic centimeter of 1 to 1000 solution adrenalin is injected subcutaneously and subsequent observations are made upon pulse-rate, blood-pressure, urinary secretion, blood sugar and objective and subjective symptoms. It has served a great purpose in our clinic, not only from a diagnostic and prognostic standpoint concerning thyroid conditions, but it has increased our interest in endocrin disturbances in general.

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[10] Am. Jour. Physiol., October, 1919.

[11] The Isolation in Crystalline Form of the Compound Containing Iodin Which Occurs in the Thyroid, Jour. Am. Med. Assn., 1915, lxiv, 2042.

By way of improvement in technic we would suggest that the administration of the adrenalin be preceded by a preliminary course of hypodermics of sterile water. It gives the patient time to be accustomed to the hospital, to hypodermic medication and to the routine of close observation. We find the results much more reliable when this precaution is taken. The effect of adrenalin administered in this way and for this purpose, we feel, is subject to a number of interpretations. At present we believe we can recognize two or three rather distinct groups of cases as the result of the activating injection. One is a group in which the circulatory symptoms—tachycardia, palpitation and precordial distress—predominate; another in which the nervous symptoms, such as substernal distress, *i. e.*, globus, "internal tremor," trembling of the hands, restlessness and agitation are present, with scarcely any acceleration of the pulse-rate. And a third group, in which only disturbance of the carbohydrate metabolism occurs, as evidenced by hyperglycemia and mild glycosuria as the leading factors. In the case of the first patient whose history I presented the Goetsch test was negative in so far as an increase of the circulatory and nervous disturbances was concerned, but sugar was found in the urine, and a sugar tolerance test also produced a glycosuria and a hyperglycemia. When the patient was not under the effect of adrenalin there was no hyperglycemia..

We are of the opinion that many points will have to be cleared up before the full significance of the Goetsch test will be known. May it not be possible that with the Goetsch test we might find there is a stage in the course of the hyperthyroid condition, even preceding that of appreciably increased metabolism, in which the Goetsch test might be positive, and thus warn us of what is about to take place?

Enough has been said to justify the claim that we are in possession at present of data from the laboratory which has greatly stimulated our interest and increased our ability to recognize and diagnose early endocrin disturbances. It must be concluded that the internist who is in possession of the data to which meager reference has already been made should now be in a position to recognize the first alteration of function which points to disturbance or disease of the endocrin system, and should forestall by prophylactic measures the impending disaster. In the case of the thyroid, for example, where there is evident hypertrophy, one's attention should, of course, be called at once to the possibility of early symptoms of Graves's disease; but when there is no apparent hypertrophy the slightest symptom should receive careful consideration.

It is not the purpose of this paper to go into the details of the symptomatology, such as the definite loss of weight in spite of unimpaired appetite, the increased amount of energy discharged, the physical and mental restlessness, the tremor, the loss of vascular tone, the acceleration of the pulse-rate and the so-called internal tremor to which the thyroid patient so frequently refers. It is intended rather to call attention to very early functional changes which may be recognized by certain tests, showing an unbalanced endocrin system. If these changes are taken at their face value and early treatment instituted the results in many cases would no doubt be different. Medical treatment would be more effective and the surgeon and roentgenologist would not need to be called so frequently as they are at present. This I believe to be especially true in so far as the thyroid gland is concerned.

In a paper by Dr. John H. Musser, read in Chicago in 1911, on Problems in the Treatment of Exophthalmic Goitre,[12] he says in his conclusions: "Finally, my conviction is that the surgeon does too much and the internist too little in the treatment of goitre." This was probably the last paper Dr. Musser read. With our present knowledge we would no doubt say, in addition to what Dr. Musser has said, that the internist besides doing "too little" does it too late. Nothing will clear up the goitre problem more satisfactorily and promise better therapeutic results than prompt recognition and establishment of early, definite and earnest treatment. Under such conditions a large proportion of cases will no doubt get well with so-called medical treatment. The fact, of course, must never be lost sight of that any pathology of the thyroid gland should receive the same consideration that similar pathology does in other parts of the body, with this difference, however: The far-reaching effect of suddenly disturbing thyroid secretion must always be kept in mind. If a cyst is present, or an adenoma, or a malignant neoplasm, it should be considered along the well-established lines which such pathology receives when it occurs in other parts of the body. And on account of our lack of knowledge of the etiology of exophthalmic goitre there must be no varying from the general principles which obtain in the treatment of any disease. Particularly is this true of the chronic infections due to local foci and of the acute general infections. We could all no doubt cite instances of the apparently very close relation of thyroid disturbances to diseased tonsils, infected sinuses or abscessed teeth. Unquestionably these conditions should all be taken care of on the basis of their own pathology, whether there is thyroid disturbance or not. This means, therefore, that surgery has a large field in diseases of the endocrin system, and especially in diseases of the thyroid.

In speaking of medical treatment, on account of the peculiar individual phases which each case may represent, it is best only to mention the principles upon which it is based. It is based upon the principles established by those investigators to whom reference has been made. The disturbance of function of that nervous mechanism which Cannon, Mills and others have described must be controlled. This means rest in varying degrees. It may mean, also, very active medication, such as nerve sedatives—the bromides for example. The loss in weight which Du Bois has explained must be overcome. This means abundance of food—indeed, forced feeding. The disturbance of a certain secretion to which Marine and Kimball have called attention must be balanced by careful medication. This means measures to forestall or to correct a changed secretion. No one up to this day has better outlined a course of treatment, especially in so far as rest and forced feeding is concerned, than has Dr. S. Weir Mitchell in his plan of the rest treatment. The possibilities of restoring nerve function, mental balance and loss of weight by the proper application of the principles laid down by Mitchell is recognized by all. One need only read Mitchell's little book entitled *Fat and Blood* to get a definite outline and all the details of the rest treatment. It is especially applicable in the incipient and early cases of thyroid disturbance. The rest and feeding must be prolonged until the results are obtained and securely held.

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[12] Am. Jour. Med. Sc., cxliii, 810.

The late Dr. Janeway, in discussing a collection of papers referring to thyroid conditions and the various treatments therefor, said: "I have seen that symptoms when recognized early permit of successful medical treatment in spite of the fact that for the patients studied nowadays in hospitals surgery is usually necessary. One of the reasons for difference of opinion between surgical and medical men is that we tend more and more to treat our patients in the hospital (where they arrive late). In private patients who will early coöperate, however, the medical man may accomplish cures which are permanent. Such patients must be carefully selected and more carefully managed.[13]

This brings us to the crux of the goitre question in so far as the treatment of all cases in whatever stage is concerned. It is the proper selection of cases, or rather the proper selection of the treatment, for the particular individual patient. Unfortunately, patients do not usually consult a physician in the early stage to which attention has been called. Prophylactic treatment is not always applicable. Yet patients must be cared for at whatever stage they present themselves. Early in my medical practice I determined upon a classification of goitre patients which has been very helpful to me, and which up to the present I have not seen fit to abandon. It furnishes a rather satisfactory working basis for the determination of the proper treatment in the individual patient. It does not preclude any classification, thus far suggested, of diseases of the thyroid gland based upon demonstrable and well-recognized pathology.

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[13] Janeway, T. C.: Boston Med. and Surg. Jour., 1916, clxxv, 685.

Patients having disease or disturbance of the thyroid gland are divided into four groups:

Group 1. Those patients having hyper- or hypothyroidism without any apparent pathological change in the gland. No change in the size or shape of the thyroid is demonstrable physically. These may be early cases in which later pathology will become manifest, or they may be well-advanced cases with no pathology of the glands. If one is keen in recognizing the early symptoms of thyroid disturbance this class may be large. The symptom-complex, however, is often remarkably definite if one will go after it. At other times a study of the basal metabolism and possibly the application of the before-mentioned Goetsch test may be necessary to confirm the suspicion. The treatment in these cases is definitely medical. I do not know of any attempts of treatment by roentgen ray in these cases, unless it be in those cases in which the thymus gland is enlarged. Surgery is not necessary.

Group 2. Those patients having an enlargement of the thyroid but in which from the age of the patient and the absence of certain symptoms the diagnosis of adolescent goitre may be made. It occurs in young girls about the time of the establishment of the menstrual period. It may also occur in boys at the age of puberty. The enlargement is usually temporary. There are, of course, notable exceptions. If any definite treatment is necessary it is medical. Usually time and careful prophylactic measures may prevent the hyperthyroid syndrome. The iodides in small doses or small doses of thyroid extract may be advisable. One of my cases was a notable exception: A young girl was brought to me at the age of twelve with a slightly enlarged thyroid. It had been noticed for about four years, or since she was eight years old. Advice had already been given that it was an adolescent goitre and would likely disappear in due time. There was no reason at that time for advising anything to the contrary, as there were no symptoms. The tonsils were diseased and removed without any untoward symptoms. Definite prophylactic treatment was instituted. When the periods came on at the age of fourteen there was no change in the size of the gland, but at the end of two years it was larger. No symptoms of hyperthyroidism were noticed, but the patient wished a lobectomy for cosmetic purposes if for nothing else. A partial lobectomy was done under local anesthesia. The right lobe and the isthmus were removed. It proved to be a parenchymatous hyperplasia. Within a year of the operation the remaining lobe enlarged rapidly and symptoms of hyperthyroidism were noted. A second operation was considered, but finally it was decided to apply roentgen rays. After eighteen applications by Dr. Russell H. Boggs the swelling had about disappeared. This was three years ago. The patient lost her symptoms and seemed well. She has since been in college and has done heavy work; she had an operation for appendicitis and is living a normal life. The neck is now normal and there are no symptoms. This is undoubtedly an exceptional case, for among a large number of this group of cases this is the only one that seemed to require other than medical care. Most of these patients acquire a normal thyroid after the menstrual periods are fully established. On account of this it is extremely difficult to estimate the real value of any treatment which may be instituted.

Group 3. Those patients having an enlarged thyroid with a definite hyperthyroidism active or at times potential. The enlargement may be due to a hyperplasia of a parenchymatous type (true Graves's disease), or it may be a colloid goitre, a cyst, an adenoma or any combination of these conditions. This is a group of patients in which the course of treatment is occasionally extremely difficult to decide upon. It depends largely upon the stage of the disease or condition present at the very time the patient is seeking advice. Two principles must be kept in mind: (1) Any pathology of the thyroid should receive the same prompt consideration as similar pathology does elsewhere in the body. If the indications are for surgery it should be undertaken; if for roentgen rays the same obtains. More will be said of this when discussing group four. (2) Due regard must be given to the stage, or degree, of secretion of the thyroid gland, determined by its effect upon the general health of the patient, before deciding upon any course of treatment. In toxic goitres of extreme degree and in true exophthalmic goitres medical treatment may be the only safe treatment at first, and may be a necessary preliminary to later surgical or roentgen-ray treatment. If, after a successful course of medical treatment, the thyroid gland still presents such pathology as would ordinarily require surgical interference, surgery should be undertaken promptly, *before there is a recurrence of disturbed function.*

In certain cases the intoxication may have reached such a stage that medical treatment, *i. e.*, physical and mental rest, abundance of food, support of the circulation and nerve sedatives, however carefully prescribed, will not bring about such amelioration as to make an operation a safe procedure. Under such circumstances it may still be safe to use roentgen-ray treatment, either as a preliminary to operation or without any thought of a subsequent operation. In these cases roentgen-ray treatment has been most satisfactory. In several cases where it was begun only as a preliminary treatment the results were so satisfactory that it was continued until the symptoms subsided and the swelling practically disappeared. Of course, there are occasionally fulminating cases which run a rapid course and for which no treatment, however carefully planned, is of any avail. One such case seen some years ago was most remarkable. The patient was a child's nurse. She had charge of two children in a family. Both contracted scarlet fever and died violent deaths within a week on account of kidney complications associated with uremic convulsions. The nurse, who was very much attached to the children, harbored the idea that she was directly responsible for bringing about the contagion. She could not be convinced to the contrary and brooded continually. She had previously been perfectly well. Her pulse became rapid, the thyroid gland enlarged, the eyes protruded and tremor developed. The diagnosis was evident. Notwithstanding every care she became delirious, later comatose and died. The whole course of the disease was run in just two weeks. It will be seen that in group 3 the success of any treatment is largely dependent upon the proper selection of cases. The problem is practically the same as it is in gastric and duodenal ulcer. There are some patients who will get well with medical treatment and remain permanently well, while there are conditions in others which will interfere with recovery until surgery is undertaken, or roentgen rays are applied, and finally there are those who will not recover with any treatment. These are the fulminating cases, or the neglected chronic cases with definite vascular or nervous disturbances.

Group 4. Those patients having definite pathology of the thyroid, enlargement without any disturbances of thyroid function. This group includes malignant tumors, such as carcinomata, also the so-called "simple" goitres, or colloid growths, as well as the adenomata and cysts, and inflammatory reactions due to tubercular, luetic or other infections. They really have no disturbance of internal secretion, but may be potential cases. These are imperatively surgical conditions, especially when malignant or when producing pressure symptoms interfering with breathing or swallowing. Certain of these conditions, such as the adenomata and colloid goitres, yield satisfactorily to roentgen-ray treatment, which under certain circumstances may be preferable, but in emergency surgery is imperative.

By following such a grouping of patients as just described I have been able to advise more definitely as to the line of procedure in disease of the thyroid gland. There are, of course, border-line cases, but this occurs in any classification.

The first group includes strictly medical cases; the second group may need nothing but prophylactic care and extremely careful medication; when they need more they are already in the third group; the third group may be medical for a time and later surgical or roentgen ray or both; the fourth group is surgical always, but may present an enticing field for roentgen-ray investigation.

The physician who has only one treatment, be it medical, surgical or roentgen ray, either sees only one class of cases or fails to recognize a large class which might be successfully treated otherwise. While I would prefer to have the surgeon and the roentgenologist settle their own differences, if there are any, on this question, as an internist I feel it my duty to express an opinion. The internist usually sees the cases first, no difference what stage of the disease may be presented. If medical treatment is not indicated, or if medical treatment has failed, or under certain circumstances if it has succeeded, he should be immediately in touch with the surgeon or the roentgenologist, or both. If he is as familiar with his case as he should be, he will go into such a consultation with pretty definite convictions. From my own experience I would say as between surgery and roentgen ray, that the former has a far larger field of application, and in skilful hands is comparatively safe. It has the added advantage of furnishing definite information, in that the tissue removed may be studied and the nature of the pathology determined. This is of the utmost importance for the future conduct of the case. The roentgenologist is necessarily frequently not altogether sure of the condition with which he is dealing.

The results of operative treatment are sometimes immediate, so that the patient is able in a short time to return to his usual life or occupation. On the other hand, the roentgen-ray treatment presents some advantages which cannot be passed by and which appeal to one very strongly. It is comparatively without danger: it leaves no scar; it is painless and gives very little inconvenience; if it is unsuccessful, surgery may be undertaken with possibly less risk.[14]

The absolute safety of the procedure may be questioned. May it not be possible by roentgen ray to destroy the function of the gland entirely, as happens in the radiation of the ovaries, and produce a myxedema? The surgeon from the time he entered this field has been reminded of the dangers of removing too much glandular substance, and there are records of unfortunate results. What assurance has the roentgenologist that he may not have similar experiences? These are some of the questions which concern the internist especially.

In conclusion the following summary might be offered:

1. Exophthalmic goitre, or hyperthyroidism from other causes, should be recognized early and treated promptly, on lines specified.
2. The earlier it is recognized the more likely medical treatment will be sufficient and give permanent results.
3. The neglected cases, or the cases having definite pathology besides, are likely to require surgery or roentgen ray, or both. In this is included treatment with radium.
4. The roentgen-ray treatment of the enlarged thyroid presents most attractive advantages, but the indications for its use do not seem so definite yet, and the results are not so certain.
5. In hyperthyroidism the roentgenologist and the surgeon at best can only break through a vicious circle for which the internist may or may not have been responsible.

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[14] Malcolm Seymour: The advantages of Roentgen-ray Treatment, Boston Med. and Surg. Jour., 1916, clxxv, 568.